Stroke Severity Variations in a 12 Month Prospective Study Involving Sub-acute Ischemic Stroke Survivors With and Without Cognitive Impairment in Nnewi, Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author UPO designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors SCI, CI, ICE, ECO, VAE, ENE and OA managed the analyses of the study. Authors UPO, SCI and CI managed the literature searches. All authors read and approved the final manuscript.

Article Information

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ABSTRACT

Background: Stroke severity may intensify with cognitive impairments (CI), and impede functional recovery. Therefore proprioceptive neuromuscular facilitation (PNF) and task specific balance training (TSBT) was an exercise intervention package for stroke survivors with and without cognitive impairment (CI).

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Objective: To determine stroke severity variations in sub-acute ischemic stroke survivors with CI and without CI after 12 months prospective study

Methods: One hundred of 143 available sub-acute first-ever ischemic stroke survivors recruited using convenience sampling technique in a non-randomized controlled clinical trial. They were later conveniently allocated to a cognitive impaired group (CIG) and non-cognitive impaired group (NCIG). Proprioceptive neuromuscular facilitation (PNF) and task-specific neuromuscular facilitation (TSBT) interventions applied 3 times a week, 60 mins per session, for 12 months to the two groups. Data analysis was by independent t-test, and repeated measure ANOVA. The outcome measure was National Institute of Stroke Scale (NIHSS). The significance level was at $p < 0.05$.

Results: There was statistical significant ($p < 0.05$) improvement across time points in the stroke severity of CIG and NCIG with a large effect size of .773 and 0.641 after 12 months of PNF and TSBT. There was statistical significant difference between the two groups

Conclusions: Within the groups, a 12-month PNF and TSBT intervention improved stroke severity recovery in the two groups. However, there was significant variation in improvement between the two groups at 4 months of treatment and other time points probably because of effect of cognitive impairment, age differences and the significant difference between NIHSS scores at baseline.

1. INTRODUCTION

Stroke severity is a well-established predictor of outcome and it has been associated especially with short-term and not long-term survival. Although stroke severity can fluctuate during the first week, assessments at day one and day seven post stroke give day ninety post stroke and later long-term disability estimates [1]. In the Copenhagen Stroke Study which was a prospective community-based study that evaluated the outcome of stroke according to initial stroke severity and level of disability, the Scandinavian stroke Scale and Barthel Index were outcome measures. The study showed that 78% of stroke survivors had no or only mild deficits on discharge and that even the most severe cases regularly experience meaningful improvement during rehabilitation [2]. Stroke severity at onset is important in predicting the outcome of rehabilitation. People who had stroke presents varying forms of stroke severity depending on the degree of cortical assault which evolve when stroke events occur. Stroke severity is tested hours or days after stroke onset and this has helped in planning viable care for the patients. The National Health Institute of Health Stroke Scale (NIHSS) is a systematic assessment tool that provides a quantitative measure of stroke-related neurological deficit [3]. The NIHSS was originally designed as a research tool to measure baseline data from patients in acute stroke clinical trials. The scale is widely used today as a clinical assessment tool to check severity of stroke, to decide proper

treatment, and to predict patient outcome [4]. Stroke severity comprised three brands: Upper band – milder strokes; Middle band – moderate strokes and Lower band – severe strokes. Garraway et al first proposed the concept of three bands of stroke patients based upon stroke severity [5,6]. There are two types of recovery: neurological recovery and functional recovery. Neurological recovery of neurological impairments and is often the result of brain recovery/reorganization; it has been increasingly recognized as being influenced by rehabilitation. Functional recovery is an improvement in mobility and activities of daily living; it is influenced by rehabilitation. However, functional recovery is influenced by neurological recovery but is not dependent on it. As a general rule, severity of the initial deficit is inversely proportional to the prognosis of recovery. Most spontaneous recovery occurs during the first 3-6 months after the stroke. The course of recovery negatively accelerates as a function of time and is a predictable phenomenon [7]. Skilbeck et al. studied 92 stroke survivors with a mean age of 67.5 years (range= 36-89) at final assessment, either 2 or 3 years after a stroke. Most of recoveries were reported within the first 6 months, with continued but non-statistically significant recovery after 6 months [7]. This type of recovery has, until recently, been regarded as largely inaccessible to medical intervention or manipulation. Neurological deficits resulting from a stroke is often called impairments. Functional recovery refers to the improvement of independence in areas such as self-care and

mobility. Recovery depends on the patient's motivation, ability to learn and family supports as well as the quality and intensity of therapy. This type of recovery is modifiable by interventions and influenced by, but may occur independently of neurological recovery. Functional deficits are often called disabilities and measured in terms of functions such as activities of daily living. The mechanisms which account for neurological recovery after a stroke include: post-stroke edema were: Reperfusion of the ischemic penumbra; diaschisis, central nervous system (CNS) reorganization (Later Recovery) and reorganization of the brain after a stroke is dependent not only on the lesion site, but also on the surrounding brain tissue and on remote locations that have structural connections with the injured area. While a number of processes were identified as playing a role in neurological recovery following stroke, the role each play is not completely understood. Recovery from stroke is often attributed to the resolution of edema and return of circulation within the ischemic penumbra [8].

Current evidence shows a higher level of physical activity associated with a decreased risk of stroke, has beneficial effects on stroke risk factors and results in lesser stroke severity and a better long-term outcome following stroke. The human brain changes with response to various types of activities and experience through the reorganization of its neural connections. This phenomenon is known as neural plasticity. Studies over the past decade have indicated that the adult brain is structurally dynamic. Indeed, dendritic spines dynamically turn over in the adult brain and learning of novel tasks associated with further increases in spine turnover. Exercise training is an effective therapy for CNS dysfunctions like stroke, traumatic brain injuries etc. which has been applied to the clinic. Traditionally, the exercise training has been considered to improve brain function only through enhancement, compensation, and replacement of the remaining function of nerve and muscle [9,10,11].

A lot of multidisciplinary approaches are known to influence resolution of stroke severity both in the acute and chronic situations, however; effect of proprioceptive neuromuscular facilitation (PNF) and task specific balance training (TSBT) on stroke severity recovery of sub-acute Ischemic stroke survivors with cognitive impairment (CI) and without CI have not been before studied to the best of authors' knowledge. This is the gap the present study wants to fill. The current study thus aims to find if there would be comparable stroke severity variations between CI and NCI sub-acute ischemic stroke survivors after 12 months PNF and TSBT interventions. We therefore hypothesize that there would be no significant difference between the CI and non-cognitive impaired (NCI) sub-acute stroke survivors after 12 months PNF and TSBT interventions.

2. METHODS

The current study is a multi-center non-randomized controlled clinical trial involving 143 stroke survivors of ischemic subtypes with first ever cerebral ischemia. The study was delimited to ischemic stroke survivors of between 35 to 65 years of age of not less than 3 months and not more than 6 months duration. The participants' recruitment was by purposive sampling from four hospitals, Nnamdi Azikwe University Teaching Hospital, Myles Specialist Hospital, Hope Specialist Hospital and Mercy Specialist Hospital, after a neuropsychiatric test done under supervision of a neurologist. The participants had mostly cerebral ischemia of the middle cerebral artery (MCA). Based on radiological reports, participants in the present study had the highest frequency of affectation within the middle cerebral artery, at the following regions; the insula, putamen, operculum, and superior temporal cortex, as well as the inferior and superior occipito-frontal fascicles, superior longitudinal fascicle and uncinate fascicle. Participants were treated with proprioceptive neuromuscular facilitation (PNF) and task-specific balance training (TSBT) at standard facilities: Landmark Physiotherapy Services, Nnewi and Department of Physiotherapy, Nnamdi Azikiwe University Teaching Hospital, Nnewi. PNF and TSBT interventions were applied 3 times a week, 60 minutes per session, for 12 months. The study conformed to STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology)

2.1 Sample Size Calculation

The sample size was determined using a mathematical relationship recommended by Macfarlane [12]

N= 2 (Z1 + Z2)2
(ES) 2

ES= standardized difference of variable with the least possible change = mean difference

Standard deviation= 1.8/3.0= 0.60. [13]

N= sample size for a group

Z_1= percentage point of normal distribution for statistical significance level at 95% confidence Interval = 1.96

Z_2= percentage point of normal distribution for statistical power at 80% = 0.8416;

N= 2 (1.96 + 0.84)2/ (0.60) 2 = 15.68/0.36 = 43.56=44
N= 2x44= 88.

About 70% of the population was expected compliant, and an attrition rate of 30% of the calculated sample size amounting to 30/100 x 88 = 26), was added to the sample size. Therefore, N (total sample size) = 88 + 26 = 114. Initially 143 participants comprising 85 and 58 participants with and without cognitive impairments were recruited. However, only 100 participants comprising 50 stroke survivors each were allocated into cognitive impaired group (CIG) and non-cognitive impaired (NCIG) group, who eventually completed the study. We included participants with a diagnosis of ischemic stroke between the ages of 30 - 65 from 3 - 6 months since stroke onset; adjudged either cognitively or non-cognitively impaired by a neurologist using mini mental state examination; no history of other neurological (Parkinson, cognitive impairment or dementia), metabolic (severe or uncontrolled diabetes) or orthopedic conditions (severe arthritis or multiple fracture leading to significant bone loss; no recurrent or multiple cerebral infarctions; participants must resident within Nnewi North or South LGAs and; participants must read, write and understand English language.

2.2 Ethical Approval

Ethical approval from the Nnamdi Azikiwe University Teaching Hospital Ethical Committee (NAUTHEC), Nnewi, along a supervision approval from a Consultant neurologist was obtained. All the participants gave their informed consent and principles of declaration of Helsinki were adhered to. They were also assured of the confidentiality of the information they provided. It was made clear to the participants that they have the right to refuse to take part or to withdraw at any stage of the project, and these rights respected all through the research procedure.

2.3 Interventions

2.3.1 <u>Proprioceptive Neuromuscular Facilitation (PNF)</u>

The PNF technique/ strengthening program comprised rhythmic initiation, repeated contraction, slow reversal and rhythmic stabilization. Ten repetitions of each pattern were done before proceeding to the next pattern in line with what obtains in earlier PNF studies [14,15]. After the set of pattern was completed, it is repeated twice in each treatment session making 3 sets per session. This usually lasted about 30 minutes per participant per session. However, the PNF training is applied equally in terms of frequency and duration irrespective of the side affected, and the set used in the study were as described by Knott and Voss [16]. A pamphlet containing the described patterns also served as treatment guide during training [17].

The participants in the two groups (CIG and NCIG) are treated using same task specific activities parameters targeted at optimizing balance, such as:

a) A repetitive task oriented practice of sit to stand transfer – 10 repetitions
b) Aerobic training using bicycle ergometer
c) Obstacle crossing- stepping over obstacle using 5 wooden obstacles placed at 5 meters apart- 10 repetitions
d) Standing balance with eyes open using a balance board for 1 minute for 10 repetitions
e) Forward and backward and forward progression 5 repetitions, and
f) Turning task- a cylinder of 20 cm diameter and 20 cm height is placed on the ground with participant walking with feet spread apart, the participants performed a pivot turn for 10 times [18]. These tasks were made flexible according to the needs of each participant, and lasted for 60 minutes to avoid getting them fatigued. However, the duration of tasks was same irrespective of laterality. An interval of 10 minutes rest would be allowed for the participants between sets of exercises. Deep breathing exercises are performed during rest period to improve fatigue and shortness of breath. Patients were closely monitored to prevent any adverse cardiovascular or respiratory reactions as a result of the intervention. The intervention is timed with a stop watch and scheduled

between 8 am-12 pm on the appointment days. TSBT was applied one hour per session, three times a week, for 12 months. Four research assistants were trained to aid in each treatment session [18].

2.4 Aerobic Exercise Protocol

Initial aerobic exercise intensity was based on 60% of maximum heart rate achieved on a stress test. Each subject is progressed to 85% of the value over 12 months. All subjects is engaged in an aerobic warm-up of at least 5 minutes with perceived rating in the light range of Borg's rating of perceived exercise scale, following warm up, the subjects instructed to start with a ten minutes exercise which increased until the exercise intensity gets to the range of target heart rate and rate of perceived exertion (RPE) to commensurate with "somewhat hard", heart rate and RPE monitored to make sure subjects were exercising at their prescribed intensity throughout the study. Subjects were encouraged to increase their exercise time by 5 minutes each two months until they reach 50 minutes at the ninth month, which was maintained until the end of the 12 months program [18].

2.5 Outcome Measures

Mini-mental state examination was used to assess global cognition level, which comprised items on attention, language, following commands and object copying, orientation, registration and recall for all participants with a stroke history ≤ 3months minimum duration. The cutoff score was 23/24 [19]. Participants that fell below the cut off assigned to CIG group while those that scale above the cut off assigned to NCIG group.

2.6 National Institute for Health Stroke Scale (NIHSS)

NIHSS is a tool used by healthcare providers to objectively quantify the impairment caused by a stroke. The NIHSS composed of 11 items, each of which scores a specific ability between a 0 and 4. For each item, a score of 0 typically indicates normal function in that specific ability, while a higher score is indicative of some level of impairment. The individual scores from each item are summed in order to calculate a patient's total NIHSS score. The maximum possible score is 42, with the minimum score being a 0. The cut off

values are1-6 mild impairment, 7-12 moderate impairment, 13-42 severe impairment [19].

2.7 Statistical Analysis

Statistical Analysis was by SPSS version 20: Descriptive statistic of Mean± SD was used in the analysis of demographic and baseline characteristics. The raw data was tested repeated normality using Shapiro-wilks while Log Transformation is utilized to normalize the data. Analysis of Variance (ANOVA) was adopted to compare variations within each group; independent t-test to compare variations between the two treatment groups. Probability value less than 0.05 was considered statistically significant.

3. RESULTS

3.1 Summary of Figure 1

Out of 143 participants that commenced the treatment, 43 dropped out before the 6th month of the study for different reasons. Thus, in the cognitive group, 10 participants missed their follow-up appointments, 11 deaths were recorded as serious adverse events; while 14 others tended towards dementia. The non-cognitive group had 6 participants who missed their follow up appointments, 2 deaths were reported as serious adverse event. Thus, only 100 participants completed the study. In the cognitive group, 58.82% completed the study; 41.18% did not complete the study. This contrasts with 86.21% who completed the study and the 13.79% who did not complete the study in the noncognitive group.

3.2 Summary of Table 1

The baseline characteristics in table 1 showed the number of male and female participants were 23(46%) and 27(54%), respectively, for the cognitive group, while the non-cognitive had 22(34%) and 28(56%) for the males and females, respectively. Their mean age differed significantly (p<0.05) and was recorded as 53.94±9.316years and 49.30±12.214years for the cognitive and non-cognitive groups, respectively. However, the duration of stroke and body mass index were not significantly different (p>0.05) for the groups. The both types of stroke were common among the traders (business men) and civil servants with professional workers having least incidence of stroke. The other

physical characteristics of the participants are presented in Table 1.

3.3 Summary of Table 2

The Mauchly's test indicated that assumption of sphericity had been violated by the NIHSS scores for cognitive group, therefore degrees of freedom was corrected using Greenhouse Geisser estimates of sphericity. The mean scores for NIHSS scores were statistically significantly different: (F (1.589, 77.837) = 166.840, $p < 0.001$. The result shows there was statistical significant decrease in NIHSS scores of cognitive impaired stroke survivors after 12 months PNF and Task specific Balance Training. The partial eta squared (effect size) was large = .773.

The mauchly's test indicated that assumption of sphericity had been violated by the NIHSS scores for non-cognitive group, therefore degrees of freedom was corrected using Greenhouse Geisser estimates of sphericity. The mean scores for NIHSS scores were statistically significantly different: (F (1.800, 87.205) = 87.677, $p < 0.001$. The result shows there was statistical significant decrease in NIHSS scores across time points in non-cognitive group. The partial eta squared (effect size) was large = .641.
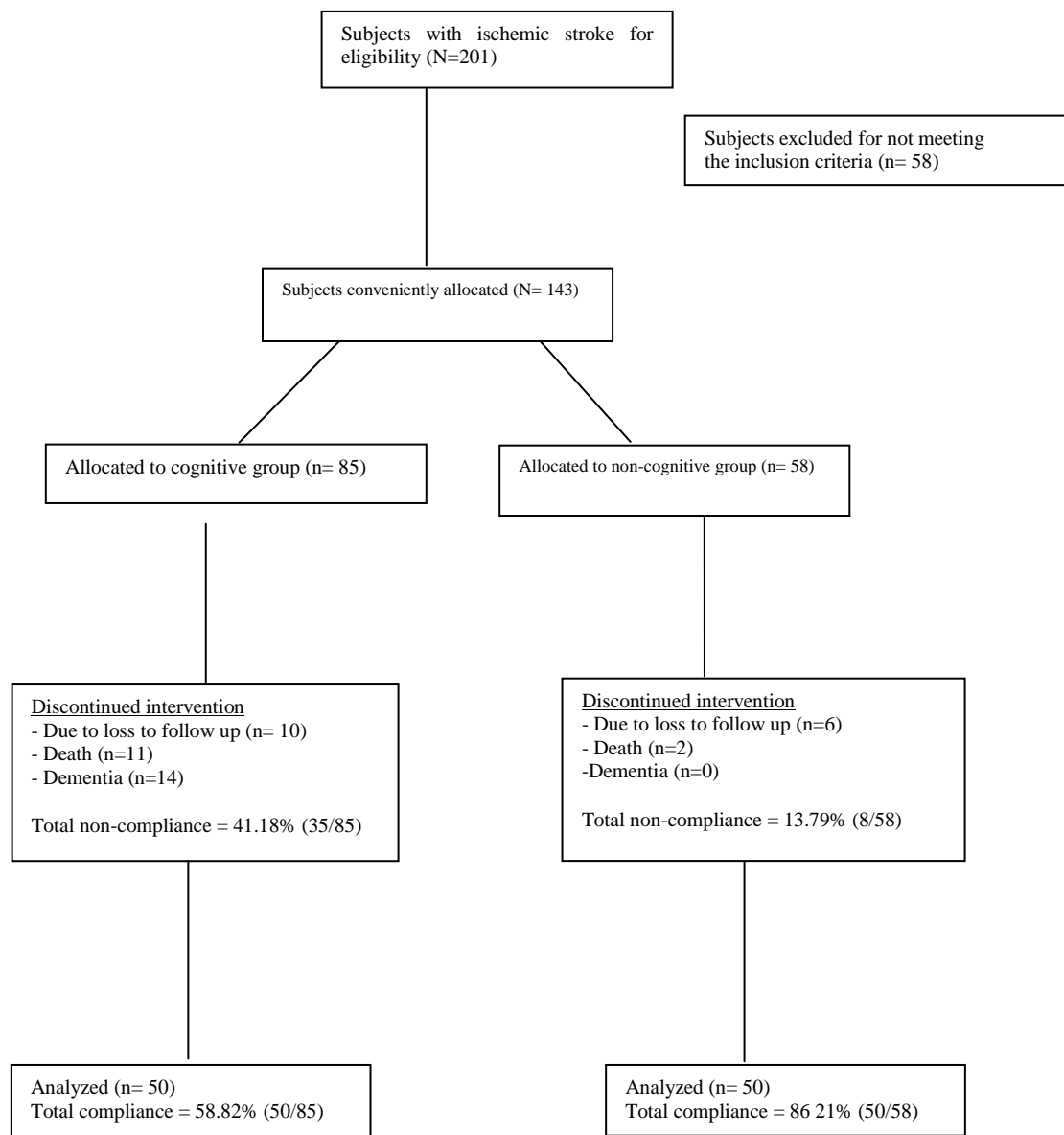

Figure. 1. Subject selection flow chart [18]

3.4 Summary of Table 3

There was a significant difference in NIHSS scores for cognitive group: 17.816 ± 6.030 and non-cognitive group: 8.080 ± 3.213; t (97) = 10.054, p = 001 at baseline. There was also significance difference in NIHSS mean scores for Cognitive: 6.306 ± 3.362 and non-cognitive: 3.680 ± 1.596; t (97) = 4.981, p = .001 across time points after 12 months intervention.

Table 1. Baseline characteristics of participants

Characteristic	Cognitive	Non-cognitive	p- value
Number(n)	50	50	
Age	53.94 ± 9.316	49.30 ± 12.214	.041*
Male	23 (46%)	22 (34%)	
Female	27 (54%)	28 (56%)	
Duration (months)	3.96 ± 1.029	4.04 ± 1.106	.928
Height	1.706 ± .0699	1.711 ± .0453	
Weight	78.760 ± 5.635	79.760 ± 6.1397	
BMI(kgm2)	27.20 ± 2.80	27.196 ± 2.80	.863
Ischemic			
Left (%)	30 (60%)	18(36%)	
Right (%)	20 (40%)	32 (64%)	

Indicates significant difference at α = 0.05, BMI=Body Mass Index

Table 2. Repeated analysis of variance (ANOVA) was adopted to compare variations within each group after 12 months PNF and TSBT

Period	Type	Mean ± SD raw	Mean ± SD transformed	Mean diff.	% Change	P-value	Conf. inter.
Baseline-4Months	CIG	17.700±6.025 12.100±4.464	1.222 ± .157 1.052 ± .1684	5.600	31.638	.001	3.928- -7.272
Baseline 4 Months	NCIG	8.080±3.212 6.580±3.289	.8701 ± .1913	1.500	18.564	.001	.770- -2.230
B/ 12 months	CIG	17.700±6.025 6.260±3.343	1.222 ± .158 .742 ± .217	11.440	64.633	.991	.9.396- -13.484
B/ 12 months	NCIG	8.080±3.212 3.680±1.596	.8701 ± .1913 .5369 ± 1539	4.400	54.455	.001	3.428 - -5.372
4/ months 8months	CIG	12.100±4.464 7160±3.792	1.052 ± 1684 .790 ± .229	4.940	40.826	.001	3.790 - -6.090
4 months/ 8 months	NCIG	6.580± 3.289 3.980 ± 1.571	.767 ± .215 .570 ± .161	2.600	39.313	.001	1.606 - -3.594
8 months/ 12 months	CIG	7.160±3.792 6.260±3.34	.796 ± .229 .742 ± .217	.900	12.569	.001	.251- -1.549
8 months/ 12 months	NCIG	3.980± 1.571 3.680 ± 1.596	.570 ± .161 .537 ± .154	.300	7.537	.001	-.087 – -687

Values are presented as the mean standard deviation. Significant difference at α = 0.05, CIG= cognitive impaired group, NCIG= Non cognitive impaired group

Table 3. Independent t-test for comparison of means at baseline to 12th month for cognitive impaired and Non-cognitive impaired groups

Type	NIHSS0	NIHSS4	NIHSS8	NIHSS12
CIG	17.816 ± 6.030	12.163±4.488	7.204±3.819	6.306±3.362
NCIG.	8.080±3.213	6.580±3.289	3.980±1.571	3.680±1.596
t-value	10.054	7.070	5.513	4.981
p.value	.001	.050	.001	.001
Confidence Interval	7.814 – 11.658	4.016 – 7.151	2.063 – 4.385	1.579 – 3.673

Indicates significant difference at α = 0.05, NIHSS0= National Health Institute Scale at baseline, NIHSS4= National Health Institute Scale at 4 months, National Health Institute Scale at 8th month, NIHSS12= National Health Institute Scale at 12th month, CIG= cognitive impaired group, NCIG= Non cognitive impaired group

4. DISCUSSION

The study was undertaken to explore the effect of PNF and TSBT on the stroke severity of CI and NCI stroke survivors after 12 months of intervention. The findings show that there was significant improvement in the stroke severity of cognitive impaired stroke survivors after four months of exercise intervention and other time points. Similarly there was significant improvement in the stroke severity of non-cognitive impaired stroke survivors after four months of exercise intervention and other time points. The effect sizes of the two groups was large (CIG .773 and NCIG .461) making the interventions clinically significant. The reduction in stroke severity as shown in the NHISS scores in table 2 might be linked to influence of exercises in bringing about cortical reorganization/neural plasticity which helped to relieve stroke severity after spontaneous recovery window (3-6 months). A key aspect of neuroplasticity that has important implications for rehabilitation is change in neuronal networks that are use-dependent. Animal experimental studies and clinical trials in humans have shown that forced use and functional activities lead to improved function [20]. On the other hand, techniques that promote nonuse may inhibit recovery. This believes collaborated the finding that prolonged lack of active movement following cortical injury may lead to subsequent loss of function in adjacent, undamaged regions of the brain (Animal study) [21]. In the past, the conventional 'wisdom' was that benefits from rehabilitation was achieved primarily through training patients in new techniques that compensate for impairments such as, using the uninvolved hand to achieve self-care independence. This approach avoided intense therapy on the weak upper limb. Currently, it is recognized that repeated participation by patients in active physical therapeutic programs probably provides direct influence on the process of functional reorganization in the brain and enhances neurologic recovery [20].

The baseline characteristics revealed a total of 100 ischemic stroke survivors (50 cognitive and 50 non-cognitive) completed this research study. The ratio of the male to female was almost same in the two groups; therefore, the differences in sex were consistent and indicative of similarity of the samples in this context. It was further revealed that duration of stroke and the body mass index were not significantly different (p>0.05).

Stroke severity as measured by NIHSS showed a steady improvement (decline in NIHSS scores) in within group analysis from baseline to 12months in CIG stroke survivors after 12 months PNF and TSBT. The implication to the study is that both the neurological recovery engendered by spontaneous recovery, and the functional recovery engendered by cortical reorganization and neuroplasticity are important for determining stroke severity outcomes. It is pertinent to infer that the recovery of stroke severity recorded between baseline and 4th month in the two groups may be attributed to spontaneous recovery more than the intervention given. A reduction in neurological impairment can result from spontaneous, natural neurologic recovery (via the effects of treatments that limit the extent of the stroke) or from other interventions that enhance neurologic functioning. A patient demonstrating neurologic recovery presents with improvements in motor control, language ability, or other primary neurologic functions [20]. The initial recovery from stroke is often attributed to resolution of edema and return of circulation within the ischemic penumbra [8]. Between 4th month and 8th month there was a significant improvement (NIHSS decline) in the stroke severity in the two groups. The course of this recovery may be attributed to the effects of both the neurological recovery and functional recovery. This finding is supported by Skilbeck et al, who opined that most spontaneous recovery occurs during the first 3-6 months after the stroke [7]. The implications being that spontaneous recovery, the effect of PNF and TSBT that elicit cortical reorganization and neural plasticity hold sway at this level of recovery of stroke severity. Also between 8th and 12th month the recovery may be entirely attributed to the effect of cortical reorganization and neural plasticity simulated by the exercise intervention. This is the point functional recovery which is mostly influenced by exercises shows dominance. The course of recovery negatively accelerates as a function of time and is a predictable phenomenon [7]. Functional recovery is influenced by neurological recovery but is not dependent on it. The implication being that the prevalence of functional recovery at this level meant that the influence of neurological recovery is almost nonexistent. Functional recovery which is a manifestation of degree of stroke severity recovery relies on the effectiveness and efficiency of exercise intervention applied. As a general rule, severity of the initial deficit is inversely proportional to the prognosis for

recovery. It is pertinent to assert that the resolution of severity of stroke is critical to level of functional recovery and independence being anticipated in a patient [22]. The level of stroke survivor's reintegration back to the society may invariably lean on the quantum of functional recovery and degree of independence attained post rehabilitation. This assertion is collaborated by the finding that initial severity of the stroke is inversely proportional to the final functional outcome, with the majority patients who suffer mild strokes demonstrating no or only mild disabilities, while the majority patients suffering very severe strokes still experience severe or very severe deficits even after the completion of rehabilitation. A number of studies have shown that recovery may continue at a slower pace for at least 6 months; with up to 5% of patients continuing to recover for up to one-year. This is especially true with patients who are severely disabled at the time of initial examination [23,24,25,26,27,28]. Significantly, progress towards recovery may plateau at any stage of recovery with only a very small percentage of those with moderate to severe strokes (about 10%) achieving 'full recovery'. The progress of recovery may however be dependent on the initial severity of stroke, how early the exercise intervention commenced, type of exercise program, age of participants and the frequency of exercise intervention program. Brain plasticity is the ability of the nervous system to modify its structural and functional organization. The two most plausible forms of plasticity are collateral sprouting of new synaptic connections and unmasking of previously latent functional pathways. Other mechanisms of plasticity include assumption of function by undamaged, redundant neural pathways, reversibility from diaschisis, denervation super sensitivity, and regenerative proximal sprouting of transected neuronal axons. Experimental evidence indicates that plasticity can be altered by several external factors, including pharmacologic agents, electrical stimulation, and environmental stimulation [21].

A comparison of the two groups using independent t-test revealed a significant difference in recovery of stroke severity at 4th month, 8th month and 12th month after exercise interventions. The outcome leads to rejection of study hypothesis which states that there will be no significant difference in stroke severity recovery variations in CIG and NCIG after 12 months exercise intervention. Consequentially the two groups presented with two levels of

stroke severity at baseline; this could have contributed to significant difference between the two groups at baseline in table 3. The implication to study is that severity of stroke in the two groups across time points might be influenced not only by the cognitive status of the study participants in the control group but also by the severity of stroke at baseline and differences in age between the two groups. This is consistent with the findings of America Heart Association in a prospective pilot study, that baseline NIHSS score was essential for prediction of acute ischemic stroke outcomes, followed by age; because traditional comorbidity index contributed little to the overall model. It concluded by recommending that studies of stroke outcomes between different care systems will benefit from including a baseline NIHSS score [29].

A preliminary data in humans and evidence from animal studies suggest that improving brain function would need 3-6 months of moderate to high intensity training. In contrast, preservation of function is best demonstrated with prolonged regimes where mild to moderate levels are more practical [30]. This agrees with the finding that the cumulative effects of the length, the intensity and the frequency of exercise training via PNF and TSBT over 1 year could trigger production of the brain-derived neurotrophic factor (BDNF) which possesses the extraordinary capacity to enhance neuronal excitability and synaptic plasticity by interacting with energy metabolism, thereby supporting cognitive abilities. Brain-derived neurotrophic factor is a member of the neurotrophin family; a group of proteins involved in neuroprotection, neurogenesis, and neuroplasticity, and has been identified as a key mediator of motor learning and rehabilitation after stroke [17].

The authors wish to appreciate that half of the patients with a first-ever lacunar infarct have mild cognitive impairment of subcortical vascular features and its presence may be a predictor of subcortical vascular dementia in the medium-long term which will impact negatively on stroke severity. Even though cognitive dysfunction in lacunar stroke patients may commonly be overlooked in clinical practice but presumed as important as motor and sensory sequelae [31,32]. We advocate that as a future line of research analysis of stroke severity not only in first-ever strokes, but also in recurrent strokes. This is necessary as cognitive impairment is a frequent finding in patients with multiple lacunar infarction recurrences and it is associated with

increased risk of cognitive impairment of vascular type. [33].

5. CONCLUSIONS

The significant variation in stroke severity recovery between the two groups was influenced by differences in stroke severity, age and cognitive impairment at baseline. These cofounders lead to rejection of the hypothesis when the two groups were compared. However, there might be some other cofounders which influenced stroke severity recovery in this current study. The implication for rehabilitation is that stroke severity recovery may not translate to direct functional improvement if cognitive impairment, stroke severity and age of the sub-acute stroke survivors are significantly different ($p < 0.05$) at baseline.

6. LIMITATIONS OF STUDY

The current work was limited by the high level of drop-outs from the cognitive group and by the limited number of participants. However, there were significant age differences between the two groups which were not unexpected considering the subjects were not randomly selected. This might be a weakness for the study design, as age might be an important confounding variable for stroke severity recovery. Perhaps, these differences between the groups may add to the explanations that in-between group analysis there was significant differences in the outcome measures across both groups. This could be sign that age-related differences and cognitive dysfunction may have suppressed gains in stroke severity recovery when PNF /TSBT were given to the cognitive impaired stroke survivors. Other limiting factors include the significant difference between the NHISS scores at baseline. This in addition to age differences at baseline was important cofounding variables in the current research that might have created the variations in stroke severity between CI and NCI.

7. RECOMMENDATIONS

More studies that will control the effects of stroke severity and age related differences at baseline are advocated. PNF and TSB would be helpful in management of sub-acute ischemic stroke survivors as their influence in eliciting cortical reorganization and neuroplasticity in reducing stroke severity especially when the effect of spontaneous recovery stopped or diminished between 3 and 6 months.

8. AVAILABILITY OF DATA AND MATERIAL

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

The trial number is PACTR 201877164763571

9. CONSENT AND ETHICS APPROVAL

Ethics approval was obtained from the Nnamdi Azikiwe Univerity Teaching Hospital Ethics Committee and informed consent obtained from participants before the commencement of the study

10. ACKNOWLEDGEMENT

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Murray GD, Barer D, Choi S, Fernandes H, Gregson B, et al. Design and analysis of phase III trials with ordered outcome scales: the concept of the sliding dichotomy. J Neurotra uma. 2005;22:511-517.
2. Middleton S, McElduff P, Ward J, Grimshaw J, Dale S, et al. Implementation of evidence-based treatment protocols to manage fever, hyperglycaemia, and swallowing dysfunction in acute stroke (QASC): A cluster randomised controlled trial. Lancet. 2011;378:1699-1706.
3. Ovbiagele B, Lyden PD, Saver JL. Disability status at 1 month is a reliable proxy for final ischemic stroke outcome. Neurology. 2010;75:688–692. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995;333:1581–1588.
4. Saver JL, Altman H. Relationship between neurologic deficit severity and final functional outcome shifts and strengthens during first hours after onset. Stroke. 2012; 43:1537–1541.
5. Garraway WM, Akhtar AJ, Smith DL, Smith ME. The triage of stroke rehabilitation. J

Epidemiol Community Health. 1981;35:39-44.

6. Garraway M. Stroke rehabilitation units: Concepts, evaluation, and unresolved issues. Stroke. 1985;16:178-181.

7. Skilbeck CE, Wade DT, Hewer RL, Wood VA. Recovery after stroke. J Neurol Neurosurg Psychiatry. 1983;46:5-8.

8. Dombovy ML. Stroke. Clinical course and neurophysiologic mechanisms of recovery. Critical Reviews in Physical and Rehabilitation Medicine. 1991;2(17):171-188.

9. Lee IM, Hennekens CH, Berger K, Buring JE, Manson JE. Exercise and risk of stroke inmale physicians. Stroke. 1999;30:1-6.

10. Deplanque D, Masse I, Lefebvre C, Libersa C, Leys D, et al. Prior TIA, lipid-lowering drug use, and physical activity decrease ischemic stroke severity. Neurology. 2006;67:1403-1410.

11. Stroud N, Mazwi TML, Case LD. Pre-stroke physical activity and early functional status after stroke. J Neurol Neurosurg Psych. 2009;80:1019-1022.

12. Macfarlane TV. Sample Size Determination for Research Projects. British Orthodontic Society. 2003;30(2):99-100.

13. Yatar GI, Yildrim SA. Wii fit balance training or progressive balance training in patients with chroninc stroke: A randomized controlled trial. Journal of Physical Therapy Science. 2015;27:1145-1151

14. Duncan P, Studenski S, Richards L, Gollub S, Lai SM, Reker D, Pererra S, Yates J. Koch V, Rigler S, Johnson D. Randomized clinical trial of therapeutic exercise in subacute stroke. Stroke. 2003;34:2173-2180.

15. Duncan P, Richards L, Wallace D, Stoker-Yates J, Pohl P, Luchies C, Ogle A, Studenski S. A randomized, controlled pilot study of a home-based exercise programme for individuals with mild and moderate stroke. Stroke. 1998;29:2055-2060.

16. Knott M, Voss DE. Proprioceptive facilitation: Patterns and techniques. New York. Harper and Row, Publishers. (3rd Edition); 1985.

17. Akosile C0, Adegoke BOA, Johnson OE, Maruf FA. Effects of proprioceptive neuromuscular facilitation technique on the functional ambulation of stroke survivors. Journal of the Nigeria Society of Physiotherapy. 2011;18-19.

18. Okonkwo UP, Okoye GC, Ezeukwu AO, Nwankwo MJ, Egwuonwu VA, et al. Cognitive recovery outcome in a 12 month quasi experimental study involving sub-acute stroke survivors in selected hospitals in Nnewi, Anambra State, Nigeria. Asian Journal of Medicine and Health. 2017;7(4): 1-12. [Article no.AJMAH.36206]

19. Salter K, Jutai J, Zettler L, Moses M, Maclure AFoley N, Teasell R. Outcome measure in stroke rehabilitation. EBRSR. 2011;34.

20. Auri B. Motor recovery in stroke. Physical Medicine and Rehabilitation. Medscape; 2016. Available:https://emedicine.medscape.com/article/324386-overview

21. Nudo RJ, Wise B, Si Fuentes F, Milliken G Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. Science. 1996;272: 1791-1794.

22. Nudo RJ. Adaptive plasticity in motor cortex: Implications for rehabilitation after brain injury. J Rehabil Med. 2003;(Suppl-41):7-10.

23. Bonita R, Beaglehole R. Recovery of motor function after stroke. Stroke. 1988;19(12): 1497-500.

24. Duncan PW, Goldstein LB, Matchar D, Divine GW, Feussner J. Measurement of motor recovery after stroke. Outcome assessment and sample size require-ments. Stroke. 1992;23:1084-1089.

25. Ferrucci L, Bandinelli S, Guralnik JM, Lamponi M, Bertini C, Falchini M, Baroni A. Recovery of functional status after stroke. A post-rehabilitation follow-up study. Stroke. 1993;24:200-205.

26. Kelly-Hayes M, Wold PA, Kase CS, Gresham GE, Kannell WB, D'Agostino RB. Time course of functional recovery after stroke: The Framingham study. J Neurol Rehabil. 1989;3:65-70.

27. Wade DT, Langton-Hewer R, Wood VA, Skilbeck CE, Ismail HM. The hemiplegic arm after stroke: Measurement and recovery. J Neurol Neurosurg Psychiatry. 1983;46:521-524.

28. Wade DT, Wood VA, Heller A, Maggs J, Langton HR. Walking after stroke. Measurement and recovery over the first 3 months. Scand J Rehabil Med. 1987;19: 25-30.

29. Rost NS, Alex B, Jin-Moo L, Marc R, Steven M, Louise S, et al. Stroke severity

Is a crucial predictor of outcome: An international prospective validation online. America Heart Association. J Am Heart Assoc. 2016;5:e002433.
DOI: 10.1161/JAHA.115.002433

30. Narayanasetti PTN, Thomas PTA. Exercise and neural plasticity– a review study. J Neurol Neurosci. 2017;8(5):216.
DOI: 10.21767/2171-6625.1000216

31. Jacova C, Pearce LA, Costello R, McClure LA, Holliday SL, Hart RG, Benevento OR. Cognitive impairment in lacunar strokes:

The SPS3 trial. Ann Neurol. 2012;72:351–362.
Available:https://doi.org/10.1002/ana.23733

32. Yaffe K, Falvey C. Cerebral small vessel disease. J Neurol Sci. 2007;257:160–165.

33. Arboix A, Font A, Garro C, García-Eroles L, Comes E, Massons J. Recurrent lacunar infarction following a previous lacunar stroke: A clinical study of 122 patients. J Neurol Neurosurg Psychiatry. 2007;78(12): 1392–1394.